Your wildcard search against 2000 terms has yielded the results below

Search for additional matches among the next 2000 terms

starting with: ANTIBOD$(ANTIBODY-VIRUS-LABELED).P25-P81,P20-P24,P17-P19,P1-P15,P16-P16.

Search Results -

Terms	Documents
l4 and antibod$	8

Database: US Patents Full-Text Database; JPO Abstracts Database; EPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

Refine Search: `l4 and antibod$` Clear

Search History

Today's Date: 7/20/2000

DB Name	Query	Hit Count	Set Name
USPT,JPAB,EPAB,DWPI,TDBD	l4 and antibod$	8	L5
USPT,JPAB,EPAB,DWPI,TDBD	l3 and metastasis	22	L4
USPT,JPAB,EPAB,DWPI,TDBD	l2 and cancer	44	L3
USPT,JPAB,EPAB,DWPI,TDBD	MORI-H$.in.	7579	L2
JPAB	08225457	1	L1

Search Results -

Terms	Documents
encapsulation near BGG	0

Database: US Patents Full-Text Database; JPO Abstracts Database; EPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

Refine Search: [ ] Clear

Search History

Today's Date: 7/20/2000

DB Name	Query	Hit Count	Set Name
USPT	encapsulation near BGG	0	L15
USPT	encapsulation near KLH	0	L14
USPT	encapsulation near BSA	4	L13
USPT	l11 and (tumor or cancer)	24	L12
USPT	l9 and lipid	49	L11
USPT	l9 and (lipid near BGG)	0	L10
USPT	BGG and vaccine	102	L9
USPT	lipid near vaccine	14	L8
USPT	l5 and (tumor adj vaccine)	47	L7
USPT	l5 and tumor vaccine	14212	L6
USPT	l4 and lipid	8068	L5
USPT	B2-glycoprotein I and cancer	31026	L4
USPT	lipid/polypeptide	1	L3
USPT	lipid adj polypeptide	17	L2
USPT	4983397.pn.	1	L1

```
=> file medline biosis embase cancerlit

COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.15       0.15

FILE 'MEDLINE' ENTERED AT 16:39:51 ON 20 JUL 2000

FILE 'BIOSIS' ENTERED AT 16:39:51 ON 20 JUL 2000
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FILE 'EMBASE' ENTERED AT 16:39:51 ON 20 JUL 2000
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FILE 'CANCERLIT' ENTERED AT 16:39:51 ON 20 JUL 2000

=> s lipid/protein or lipid/polypeptide

'PROTEIN' IS NOT A VALID FIELD CODE
'POLYPEPTIDE' IS NOT A VALID FIELD CODE
'PROTEIN' IS NOT A VALID FIELD CODE
'POLYPEPTIDE' IS NOT A VALID FIELD CODE
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'PROTEIN' IS NOT A VALID FIELD CODE
'POLYPEPTIDE' IS NOT A VALID FIELD CODE
L1             0 LIPID/PROTEIN OR LIPID/POLYPEPTIDE

=> s lipid protein or lipid polypeptide

L2          7752 LIPID PROTEIN OR LIPID POLYPEPTIDE

=> s (cancer or tumor) and vaccine

L3         27174 (CANCER OR TUMOR) AND VACCINE

=> s l2 and l3

L4             1 L2 AND L3

=> d ibib abs


L4   ANSWER 1 OF 1  EMBASE  COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER:   94156778  EMBASE
DOCUMENT NUMBER:    1994156778
TITLE:              Vesicles for tumour-associated antigen presentation to
                    induce protective immunity: Preparation, characterization
                    and enhancement of the immune response by
immunomodulators.
AUTHOR:             Bergers J.J.; Den Otter W.; Crommelin D.J.A.
CORPORATE SOURCE:   Department of Pharmaceutics, Utrecht Institute of
                    Pharmaceutical, Utrecht University, PO Box 80.082,3508 TB
                    Utrecht, Netherlands
SOURCE:             Journal of Controlled Release, (1994) 29/3 (317-327).
                    ISSN: 0168-3659  CODEN: JCREEC
COUNTRY:            Netherlands
DOCUMENT TYPE:      Journal; Conference Article
FILE SEGMENT:       016     Cancer
```

026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Tumour-associated antigens (TAA) that are expressed on tumour cells can induce resistance to tumour transplants in immunized syngeneic hosts. In this report three issues related to tumour **vaccines** are discussed. (1) Solubilization of TAA from tumour cells and their presentation on a membrane-like structure to the immune system. Proteins and lipids were solubilized from crude membranes of SL2 lymphosarcoma cells with octylglucoside (OG). By removal of OG from the OG-**lipid -protein** micelles, vesicles (0.13 um) consisting of cell membrane constituents were formed. These vesicles were used to immunize DBA/2 mice against a challenge with syngeneic SL2 cells. Specific, protective tumour immunity was observed. (2) The tumour rejection potential of these vesicles was stimulated by addition of the immunomodulators muramyl tripeptide phosphatidylethanolamine (MTP-PE) and/or interleukin-2 (IL-2). Moreover, the effect of liposome encapsulation of IL-2 on its immunomodulating effect was investigated. (3) Attention was paid to physically and chemically characterize the formulations to improve reproducibility of the antitumour effect. Finally, the loading capacity of liposomes for the cytokine IL-2 was optimized by increasing the electrostatic interaction between the liposomal bilayer and IL-2.

=> d his

(FILE 'HOME' ENTERED AT 16:39:36 ON 20 JUL 2000)

FILE 'MEDLINE, BIOSIS, EMBASE, CANCERLIT' ENTERED AT 16:39:51 ON 20 JUL 2000

L1 0 S LIPID/PROTEIN OR LIPID/POLYPEPTIDE
L2 7752 S LIPID PROTEIN OR LIPID POLYPEPTIDE
L3 27174 S (CANCER OR TUMOR) AND VACCINE
L4 1 S L2 AND L3

=> lipid peptide vaccine

LIPID IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s lipid peptide vaccine

L5 0 LIPID PEPTIDE VACCINE

=> s lipopeptide

L6 2069 LIPOPEPTIDE

=> s l6 and l3

L7 32 L6 AND L3

=> dup rem l7

PROCESSING COMPLETED FOR L7
L8 17 DUP REM L7 (15 DUPLICATES REMOVED)

=> d ibib abs 1-17

L8 ANSWER 1 OF 17 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000178497 EMBASE
TITLE: Generation of cellular immune responses to antigenic **tumor** peptides.
AUTHOR: Pietersz G.A.; Apostolopoulos V.; McKenzie I.F.C.
CORPORATE SOURCE: G.A. Pietersz, Austin Research Institute, Studley Rd., Heidelberg, Vic. 3084, Australia. g.pietersz@ari.unimelb.edu.au
SOURCE: Cellular and Molecular Life Sciences, (2000) 57/2 (290-310).
Refs: 181
ISSN: 1420-682X CODEN: CMLSFI
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 026 Immunology, Serology and Transplantation
016 Cancer
004 Microbiology
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB **Tumor** immunotherapy is currently receiving close scrutiny. However, with the identification of **tumor** antigens and their production by recombinant means, the use of cytokines and knowledge of major histocompatibility complex (MHC) class I and class II presentation had provided ample reagents for use and clear indications of how they should be used. At this time, much attention is focused on using peptides to be presented by MHC class I molecules to both induce and be targets for CD8+ cytolytic T cells. Many peptides generated endogenously or given exogenously can enter the class I pathway, but a number of other methods of entering this pathway are also known and are discussed in detail herein. While the review concentrates on inducing cytotoxic T cells (CTLs), it is becoming increasingly apparent that other modes of immunotherapy would be desirable, such as class II presentation to induce increased helper activity (for CTL), but also activating macrophages to be effective against **tumor** cells.

L8 ANSWER 2 OF 17 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 1999164996 MEDLINE
DOCUMENT NUMBER: 99164996
TITLE: **Lipopeptide** particles as the immunologically active component of CTL inducing **vaccines**.
AUTHOR: Tsunoda I; Sette A; Fujinami R S; Oseroff C; Ruppert J; Dahlberg C; Southwood S; Arrhenius T; Kuang L Q; Kubo R T; Chesnut R W; Ishioka G Y
CORPORATE SOURCE: Department of Neurology, University of Utah School of

Medicine, Salt Lake City 84132, USA.
CONTRACT NUMBER: NS34497 (NINDS)
AI42525 (NIAID)
AI35198 (NIAID)
+
SOURCE: VACCINE, (1999 Feb 26) 17 (7-8) 675-85.
Journal code: X60. ISSN: 0264-410X.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199907
ENTRY WEEK: 19990705
AB Using a bipalmitoylated **lipopeptide** consisting of an ovalbumin helper T-cell epitope covalently linked to an influenza virus cytotoxic T-lymphocyte (CTL) epitope, we addressed possible factors that may be critical for CTL induction. Antigen processing of **lipopeptide** appears to be required for T-cell induction since there was virtually no in vitro binding of **lipopeptide** to purified MHC molecules. A major portion of **lipopeptide** immunogenicity was due to its particulate nature inasmuch as CTL induction in mice correlated with insoluble **lipopeptide** constructs, whereas more soluble analogs were significantly less immunogenic. Immunohistological analysis of tissue from immunized animals revealed that **lipopeptide** migration from the s.c. injection site to the spleen could be detected as early as 1 h after immunization and cell-associated **lipopeptide** was observed on macrophages and dendritic cells, implicating both cell populations in the processing and presentation of **lipopeptide** particles to CTLs.

L8 ANSWER 3 OF 17 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999353413 EMBASE
TITLE: **Cancer** immunotherapy: Synthetic and natural peptides in the balance.
AUTHOR: Bellone M.; Iezzi G.; Imro M.A.; Protti M.P.
CORPORATE SOURCE: M. Bellone, Laboratory of Tumor Immunology, Cancer Immunother./Gene Ther. Prog., Instituto Scientifico H San Raffaele, Via Olgettina 60, 20132 Milan, Italy. m.bellone@hsr.it
SOURCE: Immunology Today, (1999) 20/10 (457-462).
Refs: 52
ISSN: 0167-5699 CODEN: IMTOD8
PUBLISHER IDENT.: S 0167-5699(99)01503-0
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Editorial
FILE SEGMENT: 026 Immunology, Serology and Transplantation
037 Drug Literature Index
016 Cancer
039 Pharmacy
LANGUAGE: English

L8 ANSWER 4 OF 17 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999002721 EMBASE
TITLE: Synthetic and immunological studies on clustered modes of mucin-related Tn and TF O-linked antigens: The preparation of a glycopeptide-based **vaccine** for clinical trials against prostate **cancer**.
AUTHOR: Kuduk S.D.; Schwarz J.B.; Chen X.-T.; Glunz P.W.; Sames D.;

Ragupathi G.; Livingston P.O.; Danishefsky S.J.
CORPORATE SOURCE: S.J. Danishefsky, Laboratory for Bioorganic Chemistry, Laboratory for Tumor Vaccinology, Sloan-Kettering Inst. for
Can. Res., 1275 York Avenue, New York, NY 10021, United States
SOURCE: Journal of the American Chemical Society, (9 Dec 1998) 120/48 (12474-12485).
ISSN: 0002-7863 CODEN: JACSAT
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The syntheses of two **tumor**-associated carbohydrate antigens, Tn and TF, have been achieved using glycal assembly and cassette methodologies. These synthetic antigens were subsequently clustered (c) and immunoconjugated to a carrier protein (KLH or BSA) or a synthetic **lipopeptide** (pam) for immunological study. Three Tn conjugates were used to vaccinate groups of mice, and all preparations proved to be immunogenic. The Tn(c) covalently linked to KLH (27-KLH) plus the adjuvant
QS-21 was the optimal **vaccine**, inducing high median IgM and IgG titers against Tn(c) by ELISA. These antibodies were strongly reactive with the Tn(c) positive human colon **cancer** cell line LS-C but not the Tn(c) negative colon **cancer** cell line LS-B by FACS. The antibodies' reactivities with natural antigens were inhibited with synthetic Tn(c) but not with structurally unrelated compounds. On the basis of these results, **vaccines** containing 27-KLH and 30-pam plus QS-21 are being tested in patients with prostate **cancer**.

L8 ANSWER 5 OF 17 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 1998298038 MEDLINE
DOCUMENT NUMBER: 98298038
TITLE: Identification of new cytotoxic T-cell epitopes on the 38-kilodalton lipoglycoprotein of Mycobacterium tuberculosis by using **lipopeptides**.
AUTHOR: da Fonseca D P; Joosten D; van der Zee R; Jue D L; Singh M;
Vordermeier H M; Snippe H; Verheul A F
CORPORATE SOURCE: Eijkman-Winkler Institute for Microbiology, Infectious Diseases, and Inflammation, Section Vaccines, Academic Hospital Utrecht, Utrecht University, 3584 CX Utrecht, The Netherlands.. D.Fonseca@lab.azu.nl
SOURCE: INFECTION AND IMMUNITY, (1998 Jul) 66 (7) 3190-7.
Journal code: GO7. ISSN: 0019-9567.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199809
ENTRY WEEK: 19980902
AB Induction of cytotoxic T lymphocytes (CTLs) by vaccination has been shown to protect against bacterial, viral, and tumoral challenge. The aim of this study was to identify CTL epitopes on the 38-kDa lipoglycoprotein from Mycobacterium tuberculosis. The identification of these CTL epitopes was based on synthesizing peptides designed from the 38-kDa

lipoglycoprotein, with known major histocompatibility complex class I (MHC-I) binding motifs (H-2Db), and studying their ability to up-regulate and stabilize MHC-I molecules on the mouse lymphoma cell line RMA-S. To improve the capacity of the identified peptides to induce CTL responses in mice, palmitic acid with a cysteine-serine-serine spacer amino acid sequence was attached to the amino terminus of the peptide. Two of five peptides with H-2Db binding motifs and their corresponding **lipopeptides** up-regulated and stabilized the H-2Db molecules on RMA-S cells. Both **lipopeptides**, in combination with incomplete Freund's adjuvant, induced CTL responses in C57BL/6 (H-2(b)) mice. Moreover, the **lipopeptide** induced stronger CTL responses than the peptide. The capacity of the various **lipopeptides** to induce CTL displayed a good relationship with the ability of the (lipo)peptide to up-regulate and to stabilize H-2Db molecules. The capacity of the peptides and **lipopeptides** to up-regulate and stabilize MHC-I expression can therefore be used to predict their potential to function as a CTL epitope. The newly identified CTL epitopes and their lipid derivatives provide us with important information for future M. tuberculosis **vaccine** design.

L8 ANSWER 6 OF 17 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 1998418922 MEDLINE
DOCUMENT NUMBER: 98418922
TITLE: Cell-mediated immunological responses in cervical and vaginal **cancer** patients immunized with a lipidated epitope of human papillomavirus type 16 E7.
AUTHOR: Steller M A; Gurski K J; Murakami M; Daniel R W; Shah K V; Celis E; Sette A; Trimble E L; Park R C; Marincola F M
CORPORATE SOURCE: Section of Gynecologic Oncology, Surgery Branch, Cancer Therapy Evaluation Program, National Cancer Institute, Bethesda, Maryland 20892, USA.. msteller@wihri.org
SOURCE: CLINICAL CANCER RESEARCH, (1998 Sep) 4 (9) 2103-9. Journal code: C2H. ISSN: 1078-0432.
PUB. COUNTRY: United States
(CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199901
ENTRY WEEK: 19990104
AB Human papillomavirus (HPV) infection has been causally associated with cervical **cancer**. We tested the effectiveness of an HLA-A*0201-restricted, HPV-16 E7 **lipopeptide vaccine** in eliciting cellular immune responses in vivo in women with refractory cervical **cancer**. In a nonrandomized Phase I clinical trial, 12 women expressing the HLA-A2 allele with refractory cervical or vaginal **cancer** were vaccinated with four E786-93 **lipopeptide** inoculations at 3-week intervals. HLA-A2 subtyping was also performed, and HPV typing was assessed on **tumor** specimens. Induction of epitope-specific CD8+ T-lymphocyte (CTL) responses was analyzed using peripheral blood leukapheresis specimens obtained before and after vaccination. CTL specificity was measured by IFN-gamma release assay using HLA-A*0201 matched target cells. Clinical responses were assessed by physical examination and radiographic images. All HLA-A*0201 patients were

able to mount a cellular immune response to a control peptide. E786-93-specific CTLs were elicited in 4 of 10 evaluable HLA-A*0201 subjects before vaccination, 5 of 7 evaluable HLA-A*0201 patients after two vaccinations, and 2 of 3 evaluable HLA-A*0201 cultures after all four inoculations. Two of three evaluable patients' CTLs converted from unreactive to reactive after administration of all four inoculations. There were no clinical responses or treatment toxicities. The ability to generate specific cellular immune responses is retained in patients with advanced cervical **cancer**. Vaccination with a lipidated HPV peptide epitope appears capable of safely augmenting CTL reactivity. Although enhancements of cellular immune responses are needed to achieve therapeutic utility in advanced cervical **cancer**, this approach might prove useful in treating preinvasive disease.

L8 ANSWER 7 OF 17 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 1999101003 MEDLINE
DOCUMENT NUMBER: 99101003
TITLE: Rapid induction of primary human CD4+ and CD8+ T cell responses against **cancer**-associated MUC1 peptide epitopes.
AUTHOR: Agrawal B; Krantz M J; Reddish M A; Longenecker B M
CORPORATE SOURCE: Biomira Inc., Edmonton, Alberta, Canada.
SOURCE: INTERNATIONAL IMMUNOLOGY, (1998 Dec) 10 (12) 1907-16. Journal code: AY5. ISSN: 0953-8178.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199905
ENTRY WEEK: 19990504
AB Antigen-specific MHC class II- and class I-restricted helper and cytotoxic
T cell responses are important anti-**cancer** immune responses. MUC1 mucin is a potentially important target for immunotherapy because of its high expression on most human adenocarcinomas. MUC1 peptide-specific type 1 T cell responses were generated in vitro using human peripheral blood lymphocytes (PBL), incubated with liposomes containing synthetic MUC1 **lipopeptide** antigen. Only two weekly stimulations with the liposomal MUC1 formulation led to the generation of potent anti-MUC1-specific T cell proliferation as well as class I-restricted cytotoxic responses. Thus the use of PBL pulsed with liposome-encapsulated
antigen provides an effective approach of rapidly generating effective antigen-presenting cell (APC) function as well as antigen specific T cells
in vitro. It may be feasible to use this technology for the rapid and effective generation of APC and/or T cells as cellular **vaccines** for adenocarcinomas.

L8 ANSWER 8 OF 17 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 1998334514 MEDLINE
DOCUMENT NUMBER: 98334514
TITLE: Liposomal formulations of synthetic MUC1 peptides: effects of encapsulation versus surface display of peptides on immune responses.
AUTHOR: Guan H H; Budzynski W; Koganty R R; Krantz M J; Reddish M A; Rogers J A; Longenecker B M; Samuel J
CORPORATE SOURCE: Faculty of Pharmacy and Pharmaceutical Sciences, University

of Alberta, Edmonton, Alberta, Canada T6G 2N8.
SOURCE: BIOCONJUGATE CHEMISTRY, (1998 Jul-Aug) 9 (4) 451-8.
Journal code: AlT. ISSN: 1043-1802.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199810
ENTRY WEEK: 19981005

AB Synthetic human MUC1 peptides are important candidates for therapeutic **cancer vaccines**. To explore whether a human MUC1 peptide BP25 (STAPPAHGVTSAPDTRPAPGSTAPP) can be rendered immunogenic by incorporation in liposomes, the effects of physical association of the peptide with liposomes on immune responses were investigated. Lipid conjugated and nonconjugated MUC1 peptides were incorporated in liposomes with a composition of distearoylphosphatidylcholine/cholesterol/dimyristoy lphosphatidylglyc erol (3:1:0.25, molar ratio) containing monophosphoryl lipid A (1% w/w of the total lipids). Liposomes were characterized for peptide retention by HPLC and for surface peptide display of MUC1 epitopes by flow cytometry. C57BL/6 mice were immunized with **lipopeptide** alone, peptide mixed with peptide-free liposomes, and peptide associated with liposomes in entrapped or surface-exposed forms. T cell proliferative responses, cytokine patterns, and antibody isotypes were studied. Results showed that immune responses were profoundly influenced by the liposome formulations. Physically associated, either encapsulated or surface-exposed, peptide liposomes elicited strong antigen-specific T cell responses, but not **lipopeptide** alone or peptide mixed with peptide-free liposomes. Analysis of the cytokines secreted by the proliferating T cells showed a high level of IFN-gamma and undetectable levels of IL-4, indicating a T helper type 1 response. Thus, physical association of the peptide with liposomes was required for T cell proliferative responses, but the mode of association was not critical. On the other hand, the nature of the association significantly affected humoral immune responses. Only the surface-exposed peptide liposomes induced MUC1-specific antibodies. A domination of anti-MUC1 IgG2b over IgG1 (94 versus 6%) was observed. Our results support the hypothesis that different immune pathways are stimulated by different liposome formulations. This study demonstrated that a liposome delivery system could be tailored to induce either a preferential cellular or humoral immune response.

L8 ANSWER 9 OF 17 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1998:158830 BIOSIS
DOCUMENT NUMBER: PREV199800158830
TITLE: Cell-mediated immunologic responses in cervical **cancer** patients immunized with a lipidated epitope of HPV-16 E7.
AUTHOR(S): Steller, Michael A. (1); Gurski, Karen J. (1); Murakami, Masaru (1); Shah, Keerti V.; Celis, Esteban; Sette, Alessandro; Chestnut, Robert W.; Trimble, Edward L. (1); Park, Robert C.; Marincola, Francesco M. (1)
CORPORATE SOURCE: (1) National Cancer Inst., Betehsda, MD USA
SOURCE: Gynecologic Oncology, (Jan., 1998) Vol. 68, No. 1, pp. 90.
Meeting Info.: Twenty-ninth Annual Meeting of the Society

of Gynecologic Oncologists Orlando, Florida, USA February 7-11, 1998 Society of Gynecologic Oncologists . ISSN: 0090-8258.
DOCUMENT TYPE: Conference
LANGUAGE: English

L8 ANSWER 10 OF 17 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 97463281 MEDLINE
DOCUMENT NUMBER: 97463281
TITLE: Activation of monocytes by three OspA **vaccine** candidates: lipoprotein OspA is a potent stimulator of monokines.
AUTHOR: Haupl T; Landgraf S; Netusil P; Biller N; Capiau C; Desmons P; Hauser P; Burmester G R
CORPORATE SOURCE: Department of Medicine III, Charite, Humboldt University, Berlin, Germany.. thomas.haeupl@rz.hu-berlin.de
SOURCE: FEMS IMMUNOLOGY AND MEDICAL MICROBIOLOGY, (1997 Sep) 19 (1) 15-23.
Journal code: BP1. ISSN: 0928-8244.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199801
ENTRY WEEK: 19980104
AB The outer surface protein (Osp) A of Borrelia burgdorferi is the first Lyme antigen to be tested in a **vaccine** for humans. Three forms of OspA **vaccine** candidates were investigated by the induction of the cytokines interleukin (IL)-1 beta, IL-6, **tumor** necrosis factor (TNF)-alpha, IL-10 and interferon (IFN)-gamma as markers of monocyte activation and immune stimulation: lipidated OspA (L-OspA), non-lipidated OspA (NL-OspA), and a fusion protein of 81 amino acids of the nonstructural protein 1 of influenza virus with OspA (NS1-OspA). All OspA preparations induced IL-1 beta, IL-6 and TNF-alpha in a concentration-dependent manner with peak levels at 12-24 h. These cytokines were entirely derived from the monocyte fraction. In peripheral blood mononuclear cells from 10 healthy donors, L-OspA at 10 micrograms ml-1 induced up to 4-fold more IL-1 beta, IL-6, and TNF-alpha than the other OspA preparations (P < or = 0.0068), followed by NS1-OspA, which was still superior to NL-OspA. L-OspA. L-OspA also induced high levels of IL-10 within 24 h but no significant amounts of IFN-gamma. This superior stimulating activity of L-OspA on unstimulated monocytes predominantly depended on N-terminal lipidation of OspA. Similarities to other lipoproteins and synthetic **lipopeptides** suggest that lipidation confers adjuvant properties on OspA. High induction of IL-10 by L-OspA further suggested a negative feedback on monocyte activation by the lipidated form. The in vitro results are in line with in vivo results in mice, monkeys and humans and indicates that lipoprotein OspA has the best potential for induction of a protective effect in humans, compared to non-lipidated antigens.

L8 ANSWER 11 OF 17 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 95277092 MEDLINE
DOCUMENT NUMBER: 95277092
TITLE: Synthetic carbohydrate **vaccines**: synthesis and immunogenicity of Tn antigen conjugates.

AUTHOR: Toyokuni T; Hakomori S; Singhal A K
CORPORATE SOURCE: Biomembrane Institute, Seattle, Washington 98119, USA..
SOURCE: BIOORGANIC AND MEDICINAL CHEMISTRY, (1994 Nov) 2 (11) 1119-32.
Journal code: B38. ISSN: 0968-0896.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199509

AB A **tumor**-associated carbohydrate antigen, Tn antigen (GalNAc alpha 1-->O-Ser), was synthesized with a spacer arm, and assembled to dimeric and trimeric structures using N-tert-butyloxycarbonyl-O-(2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-alpha- D-galactopyranosyl)-L-serine as a key building block. The synthetic antigens were conjugated with OSA and their immunogenicity examined in mice. Mice immunized with dimeric or trimeric Tn antigen showed a stronger antibody (IgM) response to a Tn-glycoprotein (asialo-ovine submaxillary mucin) than mice immunized with monomeric Tn antigen. The dimeric and trimeric Tn antigens also induced measurable IgG responses. The dimeric Tn antigen was further coupled to a Starburst dendrimer (5th generation) and to tripalmitoyl-S-glycerylcysteinyl-serine, a synthetic **lipopeptide** of the active moiety of a major lipoprotein of Escherichia coli. Unexpectedly, the Starburst dendrimer conjugate did not stimulate any immune response specific to Tn antigen. On the other hand, immunization of mice with the **lipopeptide** conjugate produced not only a high IgM response but also significant IgG anti-Tn response without any carrier molecules or additional adjuvants. The production of IgG antibody is quite significant since carbohydrate antigens are in general known to produce only IgM antibody response. Being a totally synthetic, low-molecular weight, and carrier-free immunogen, the **lipopeptide** conjugate could be a prototype of synthetic carbohydrate **vaccines**.

L8 ANSWER 12 OF 17 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 8
ACCESSION NUMBER: 1994:130593 BIOSIS
DOCUMENT NUMBER: PREV199497143593
TITLE: Synthetic **vaccines**: Synthesis of a dimeric Tn antigen-**lipopeptide** conjugate that elicits immune responses against Tn-expressing glycoproteins.
AUTHOR(S): Toyokuni, Tatsushi (1); Dean, Barbara; Cai, Shaopei; Boivin, Diane; Hakomori, Sen-Itiroh; Singhal, Anil K. (1)
CORPORATE SOURCE: (1) Biomembrane Inst., 201 Elliott Avenue West, Seattle, WA
98119 USA
SOURCE: Journal of the American Chemical Society, (1994) Vol. 116, No. 1, pp. 395-396.
ISSN: 0002-7863.
DOCUMENT TYPE: Article
LANGUAGE: English

L8 ANSWER 13 OF 17 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 9
ACCESSION NUMBER: 1993:588329 BIOSIS
DOCUMENT NUMBER: PREV199497007699
TITLE: GD3/proteosome **vaccines** induce consistent IgM antibodies against the ganglioside GD3.
AUTHOR(S): Livingston, Philip O. (1); Calves, Michele J.; Helling, Friedhelm; Zollinger, Wendell D.; Blake, Milan S.; Lowell, George H.

CORPORATE SOURCE: (1) Memorial Sloan-Kettering Cancer Cent., New York, NY 10021 USA
SOURCE: Vaccine, (1993) Vol. 11, No. 12, pp. 1199-1204. ISSN: 0264-410X.
DOCUMENT TYPE: Article
LANGUAGE: English

AB The gangliosides of melanoma and other tumours of neuroectodermal origin are suitable targets for immune intervention with tumour **vaccines**. The optimal **vaccines** in current use contain ganglioside plus bacillus Calmette-Guerin and induce considerable morbidity. We have screened a variety of new adjuvants in the mouse, and describe one antigen-delivery system, proteosomes, which is especially effective. Highly hydrophobic Neisserial outer membrane proteins (OMP) from multimolecular liposome-like vesicular structures termed proteosomes which can readily incorporate amphiphilic molecules such as GD3 ganglioside. The optimal GD3/proteosome **vaccine** formulation for induction of GD3 antibodies in the mouse is determined. Interestingly, the use of potent immunological adjuvants in addition to proteosomes augments the IgM and IgG antibody titres against OMP in these **vaccines** but GD3 antibody titres are unaffected. The application of proteosomes to enhance the immune response to GD3 extends the concept of the proteosome immunopotentiating system from **lipopeptides** to amphipathic carbohydrate epitopes such as cell-surface gangliosides. The demonstrated safety of meningococcal OMP in humans and the data in mice presented here suggest that proteosome **vaccines** have potential for augmenting the immunogenicity of amphipathic tumour antigens in humans.

L8 ANSWER 14 OF 17 MEDLINE
ACCESSION NUMBER: 93050832 MEDLINE
DOCUMENT NUMBER: 93050832
TITLE: Synthetic **lipopeptide** immunomodulators derived from bacterial lipoprotein: tools for the standardization of in vitro assays.
AUTHOR: Bessler W G
CORPORATE SOURCE: Institut fur Immunbiologie der Universitat, Freiburg, Germany..
SOURCE: DEVELOPMENTS IN BIOLOGICAL STANDARDIZATION, (1992) 77 49-56.
Journal code: E7V. ISSN: 0301-5149.
PUB. COUNTRY: Switzerland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199302

AB For the evaluation of immunomodulators by in vitro assays, agents working reproducibly are difficult to obtain; conventional preparations of bacterial immunomodulators tend to vary for different preparations. Here we suggest that synthetic **lipopeptide** analogues derived from bacterial lipoprotein can be used as standards for various in vitro assays: studying B lymphocyte activation, **lipopeptides** act as potent mitogens and polyclonal activators inducing immunoglobulin synthesis. In monocytes/macrophages, **lipopeptide** stimulate the secretion of IL-1, IL-6, **tumor** necrosis factor (TNF) and nitrogen oxide (NO); they also induce **tumor** cytotoxicity. **Lipopeptides** also constitute potent immuno-adjuvants in vitro and in vivo, either in combination with or covalently bound to antigen. These activities are displayed in various species; in mice they are found in LPS

non-responder and responder strains. The novel synthetic **lipopeptides** described here can be synthesized readily in gram amounts with high purity and reproducibility; they are non-toxic and can be stored for a long time even at room temperature. Thus, **lipopeptides** meet the requirements to serve as effective standards for a multitude of relevant biological assays.

L8 ANSWER 15 OF 17 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 90268350 EMBASE
DOCUMENT NUMBER: 1990268350
TITLE: Immunomodulatory activity of small peptides.
AUTHOR: St Georgiev V.
CORPORATE SOURCE: Department of Chemical Sciences, Division of Life Sciences,
Orion Research and Technologies Corporation, PO Box 463, Tampa, FL 33601-0463, United States
SOURCE: Trends in Pharmacological Sciences, (1990) 11/9 (373-378).
ISSN: 0165-6147 CODEN: TPHSDY
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The activity of the immune system can be modulated by a wide variety of natural and synthetic peptides. Here, Vassil St Georgiev summarizes the actions of some of the immunostimulatory and immunosuppressant small peptides that have shown most promise as therapeutics agents. Some are already in use as **vaccine** adjuvants or to prevent graft rejection. There are now indications that these peptides may also be of benefit in conditions in which the immune system is compromised, in autoimmune disease and in **cancer**.

L8 ANSWER 16 OF 17 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 89268287 EMBASE
DOCUMENT NUMBER: 1989268287
TITLE: Muramylpeptides and **lipopeptides**: Studies towards immunostimulants.
AUTHOR: Baschang G.
CORPORATE SOURCE: Pharma Research, CIBA-GEIGY AG, CH-4002 Basel, Switzerland
SOURCE: Tetrahedron, (1989) 45/20 (6331-6360).
ISSN: 0040-4020 CODEN: TETRAB
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal
FILE SEGMENT: 026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English

L8 ANSWER 17 OF 17 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 86211313 EMBASE
DOCUMENT NUMBER: 1986211313
TITLE: Immunomodulating peptides.
AUTHOR: Werner G.H.; Floc'h F.; Migliore-Samour D.; Jolles P.
CORPORATE SOURCE: Rhone-Poulenc Sante, Centre de Recherches de Vitry, F-94403
Vitry-sur-Seine Cedex, France
SOURCE: Experientia, (1986) 42/5 (521-531).

CODEN: EXPEAM
COUNTRY: Switzerland
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
026 Immunology, Serology and Transplantation
LANGUAGE: English

=> d his

(FILE 'HOME' ENTERED AT 16:39:36 ON 20 JUL 2000)

FILE 'MEDLINE, BIOSIS, EMBASE, CANCERLIT' ENTERED AT 16:39:51 ON 20 JUL 2000

L1 0 S LIPID/PROTEIN OR LIPID/POLYPEPTIDE
L2 7752 S LIPID PROTEIN OR LIPID POLYPEPTIDE
L3 27174 S (CANCER OR TUMOR) AND VACCINE
L4 1 S L2 AND L3
L5 0 S LIPID PEPTIDE VACCINE
L6 2069 S LIPOPEPTIDE
L7 32 S L6 AND L3
L8 17 DUP REM L7 (15 DUPLICATES REMOVED)

=> s l6 and (BSA or KLH or BGG)

L9 11 L6 AND (BSA OR KLH OR BGG)

=> dup rem l9

PROCESSING COMPLETED FOR L9
L10 5 DUP REM L9 (6 DUPLICATES REMOVED)

=> d ibib abs 1-5

L10 ANSWER 1 OF 5 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999002721 EMBASE
TITLE: Synthetic and immunological studies on clustered modes of mucin-related Tn and TF O-linked antigens: The preparation of a glycopeptide-based vaccine for clinical trials against prostate cancer.
AUTHOR: Kuduk S.D.; Schwarz J.B.; Chen X.-T.; Glunz P.W.; Sames D.; Ragupathi G.; Livingston P.O.; Danishefsky S.J.
CORPORATE SOURCE: S.J. Danishefsky, Laboratory for Bioorganic Chemistry, Laboratory for Tumor Vaccinology, Sloan-Kettering Inst. for Can. Res., 1275 York Avenue, New York, NY 10021, United States
SOURCE: Journal of the American Chemical Society, (9 Dec 1998) 120/48 (12474-12485).
ISSN: 0002-7863 CODEN: JACSAT
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
037 Drug Literature Index

LANGUAGE: English
SUMMARY LANGUAGE: English
AB The syntheses of two tumor-associated carbohydrate antigens, Tn and TF, have been achieved using glycal assembly and cassette methodologies. These synthetic antigens were subsequently clustered (c) and immunoconjugated to a carrier protein (**KLH** or **BSA**) or a synthetic **lipopeptide** (pam) for immunological study. Three Tn conjugates were used to vaccinate groups of mice, and all preparations proved to be immunogenic. The Tn(c) covalently linked to **KLH** (27-**KLH**) plus the adjuvant QS-21 was the optimal vaccine, inducing high median IgM and IgG titers against Tn(c) by ELISA. These antibodies were strongly reactive with the Tn(c) positive human colon cancer cell line LS-C but not the Tn(c) negative colon cancer cell line LS-B by FACS. The antibodies' reactivities with natural antigens were inhibited with synthetic Tn(c) but not with structurally unrelated compounds. On the basis of these results, vaccines containing 27-**KLH** and 30-pam plus QS-21 are being tested in patients with prostate cancer.

L10 ANSWER 2 OF 5 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 1998299466 MEDLINE
DOCUMENT NUMBER: 98299466
TITLE: Bacterial cell wall components as immunomodulators--II. The bacterial cell wall extract OM-85 BV as unspecific activator, immunogen and adjuvant in mice.
AUTHOR: Bessler W G; Huber M; Baier W
CORPORATE SOURCE: Institut fur Immunbiologie, Medizinische Fakultat der Universitat, Freiburg, Germany.
SOURCE: INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, (1997 Sep-Oct) 19 (9-10) 551-8.
Journal code: GRI. ISSN: 0192-0561.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199811
ENTRY WEEK: 19981103
AB The bacterial extract Broncho-Vaxom used for the prevention and treatment of recurrent respiratory tract infections is an immunomodulator in vitro and in vivo, as determined in a murine model. The extract acts, on the one hand, as macrophage activator and polyclonal B-lymphocyte stimulant. On the other hand, after repeated intraperitoneal or oral immunizations, the extract is immunogenic, inducing serum IgG binding to the bacterial strains used for the preparation of the extract. On bacteria, the sera recognize the cell wall components porin, lipoprotein/**lipopeptide** and murein. The bacterial extract also exhibits adjuvant properties when applied in mixture with antigens, such as TNP-**BSA** or an influenza vaccine preparation. The unspecific and the immunospecific stimulatory effect of the extract as well as its adjuvant properties could be of importance for understanding its therapeutic effect.

L10 ANSWER 3 OF 5 MEDLINE DUPLICATE 2

ACCESSION NUMBER: 96439111 MEDLINE
DOCUMENT NUMBER: 96439111
TITLE: Murine bone marrow-derived macrophages constitute feeder cells for human B cell hybridomas.
AUTHOR: Hoffmann P; Jimenez-Diaz M; Weckesser J; Bessler W G
CORPORATE SOURCE: Institut fur Immunbiologie, Albert-Ludwigs-Universitat Freiburg, Germany.
SOURCE: JOURNAL OF IMMUNOLOGICAL METHODS, (1996 Sep 13) 196 (1) 85-91.
Journal code: IFE. ISSN: 0022-1759.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199702
ENTRY WEEK: 19970204

AB Murine bone marrow-derived macrophages (BMDM), a homogeneous cell population easily obtainable in large quantities and at reproducible quality by in vitro differentiation, were used as feeder cells for human B cell hybridomas after fusion or during recloning. We used as antigens for the in vitro immunization of human B lymphocytes from peripheral blood as well as from tonsils: (i) synthetic peptides representing immunogenic sequences of gp160 and Nef of HIV-1, coupled to the **lipopeptide** carrier N-palmitoyl-S-[2,3-bis(palmitoyloxy)-(2RS)-propyl]-(R)-cysteinyl(-seryl-seryl) (P3 CSS-[gp160(303-329)] and P3C-nef24), (ii) the toxins saxitoxin and microcystin, coupled to **BSA** (**BSA**-STX and **BSA**-MCYST). After fusion with the mouse-human heteromyeloma CB-F7, we could demonstrate that BMDM exert a strong growth supporting effect on post-fusion cultures, resulting in 81.6% versus 23.6% growth-positive wells for P3C-nef24, and 100% versus 71.2% growth-positive wells for **BSA**-STX stimulated cells in cultures with and without BMDM, respectively. Furthermore, clones in wells with BMDM grew much more rapidly, resulting in 24.3% versus 3.6%, 98.1% versus 42.2% and 56.7% versus 6.7% of cultures ready for screening 2 weeks after fusion of P3C-nef24, P3CSS-[gp160(303-329)], and **BSA**-STX stimulated lymphocytes, respectively. Apart from their effect on cell growth, murine BMDM also increased the percentage of immunoglobulin (Ig)-producing cultures after fusion, as shown for **BSA**-STX stimulated lymphocytes (47.8% versus 6.7%), as well as the percentage of cultures producing specific antibodies, as demonstrated with **BSA**-MCYST activated cells (42% versus 10%). Finally, recloning efficiencies of two human B cell hybridomas (E 10 and F 2) were raised profoundly by BMDM, resulting in 100% versus 64.2% and 90.9% versus 44.2% growth-positive wells after recloning on a ten cells/well level. As murine BMDM can also be stored in liquid nitrogen without loss of activity, they constitute ideal feeder cells for the establishment of human B cell hybridomas.

L10 ANSWER 4 OF 5 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 91355710 MEDLINE
DOCUMENT NUMBER: 91355710
TITLE: Preparation of human and murine monoclonal antibodies: antigens combined with or conjugated to **lipopeptides** constitute potent immunogens for in vitro and in vivo immunizations.
AUTHOR: Hoffmann P; Jimenez-Diaz M; Loleit M; Troger W; Wiesmuller K H; Metzger J; Jung G; Kaiser I; Stocklin S; Lenzner S; et

al
CORPORATE SOURCE: Institut fur Immunbiologie der Universitat, Freiburg, FRG..
SOURCE: HUMAN ANTIBODIES AND HYBRIDOMAS, (1990) 1 (3) 137-44.
Journal code: A6A. ISSN: 0956-960X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199112
AB **Lipopeptide** analogues of bacterial lipoprotein constitute polyclonal B lymphocyte activators. Combined with or covalently coupled to antigens, they act as potent adjuvants. We could show that antigens (**BSA**-DNP, TNP-SRBC, saxitoxin, HIV-1 gp160(BH10303-329, EGFR516-523) combined with or coupled to the synthetic lipodipeptide N-palmitoyl-S-(2,3-bis(palmitoyloxy)-(2RS)-propyl)-(R)-cysteinyl-s erine (P3CS) constitute active immunogens in vivo in mice. They were also able to induce an in vitro humoral immune response in the murine and human systems, and B lymphocytes thus activated were suitable for fusion. Thus, the antigens chaperonin/phytochrome, **BSA**-saxitoxin, histamine, HIV-1 gp160 (BH10(303-329)), HIV-1 gp160 (RF316-341)), and HIV-2 p17 (ROD111-121) combined with or conjugated to P3CS could be used for in vitro immunization followed by the preparation of murine and human monoclonal antibodies. Our novel immunization procedure offers reproducibility, high antibody titers often after one immunization, lack of toxicity of the adjuvants, easy chemical preparation of the conjugates in mg amounts, and the applicability of the conjugates for screening for the antibodies obtained.

L10 ANSWER 5 OF 5 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 89335264 MEDLINE
DOCUMENT NUMBER: 89335264
TITLE: **Lipopeptide** derivatives of bacterial lipoprotein constitute potent immune adjuvants combined with or covalently coupled to antigen or hapten.
AUTHOR: Reitermann A; Metzger J; Wiesmuller K H; Jung G; Bessler W G
CORPORATE SOURCE: Institut fur Immunbiologie der Universitat, Freiburg..
SOURCE: BIOLOGICAL CHEMISTRY HOPPE-SEYLER, (1989 Apr) 370 (4) 343-52.
Journal code: AHC. ISSN: 0177-3593.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198911
AB **Lipopeptide** analogues of the N-terminus of bacterial lipoprotein consisting of N-palmitoyl-S-[2,3-bis(palmitoyloxy)-(2RS)-propyl]-(R)-cysteine (Pam3Cys) attached to one to five further amino acids [Pam3Cys-Ser-Ser-Asn-Ala, Pam3Cys-Ser-(Lys)4, Pam3Cys-Ala-Gly, and Pam3Cys-Ser] were investigated for biological activity. In vitro, the compounds proved to be potent activators for Balb/c splenocytes as determined by proliferation assays. When given in vivo in combination with SRBC, Pam3Cys-Ser and Pam3Cys-Ala-Gly acted as immunoadjuvants enhancing the antigen specific IgM response after 7, and the IgG response after 14 days. In combination with dinitrophenylated bovine serum albumin (**BSA**(Dnp)), especially the amphiphilic and water-soluble

lipohexapeptide Pam3Cys-Ser-(Lys)4 constituted a potent immune adjuvant. The **lipopeptide** was able to fully replace Freund's complete adjuvant (FCS) enhancing both anti-Dnp IgM and IgG in Balb/c mice. The hapten Dnp was also coupled directly--or via the spacer molecule 1,6-diaminohexane (HMD)--to the synthetic **lipopeptides**. The chemically defined low-molecular-mass conjugates obtained were capable of inducing anti-hapten-specific IgM and IgG without further adjuvants or carriers. The anti-hapten responses induced by these chemically uniform **lipopeptide**-hapten conjugates were, however, less pronounced than the response to the conventional heterogeneous hapten-protein conjugate **BSA**(Dnp), and only a weak boost effect was observed. Our results show that defined **lipopeptides** are novel immunoadjuvants either combined with or covalently linked to antigens or haptens.

=> d his

(FILE 'HOME' ENTERED AT 16:39:36 ON 20 JUL 2000)

FILE 'MEDLINE, BIOSIS, EMBASE, CANCERLIT' ENTERED AT 16:39:51 ON 20 JUL 2000

```
L1             0 S LIPID/PROTEIN OR LIPID/POLYPEPTIDE
L2          7752 S LIPID PROTEIN OR LIPID POLYPEPTIDE
L3         27174 S (CANCER OR TUMOR) AND VACCINE
L4             1 S L2 AND L3
L5             0 S LIPID PEPTIDE VACCINE
L6          2069 S LIPOPEPTIDE
L7            32 S L6 AND L3
L8            17 DUP REM L7 (15 DUPLICATES REMOVED)
L9            11 S L6 AND (BSA OR KLH OR BGG)
L10            5 DUP REM L9 (6 DUPLICATES REMOVED)

=> s l6 and (diphtheria toxin or B2-glycoprotein I)

L11            0 L6 AND (DIPHTHERIA TOXIN OR B2-GLYCOPROTEIN I)

=> s l6  B2-glycoprotein I

MISSING OPERATOR L6   B2-GLYCOPRO
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s  B2-glycoprotein I

L12           23 B2-GLYCOPROTEIN I

=> dup rem l12

PROCESSING COMPLETED FOR L12
L13           21 DUP REM L12 (2 DUPLICATES REMOVED)

=> s l13 and l3

L14            0 L13 AND L3

=> s  B2 glycoprotein

L15           26 B2 GLYCOPROTEIN
```

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=> s l15 and l3
L16             0 L15 AND L3
=> s Beta 2 glycoprotein I
L17          2285 BETA 2 GLYCOPROTEIN I
=> s l17 and l3
L18             0 L17 AND L3
```

FILE 'CANCERLIT' ENTERED AT 11:13:12 ON 20 JUL 2000

FILE 'EMBASE' ENTERED AT 11:13:12 ON 20 JUL 2000

FILE 'BIOSIS' ENTERED AT 11:13:12 ON 20 JUL 2000

=> s N-acetylmuramyl-L-alanyl-Disoglutaminyl?

L1 0 N-ACETYLMURAMYL-L-ALANYL-DISOGLUTAMINYL?

=> s cushman-M?/au

L2 423 CUSHMAN-M?/AU

=> s l2 and MTP-PE

L3 3 L2 AND MTP-PE

=> dup rem l3

PROCESSING COMPLETED FOR L3
L4 3 DUP REM L3 (0 DUPLICATES REMOVED)

=> d ibib abs 1-3

L4 ANSWER 1 OF 3 CANCERLIT
ACCESSION NUMBER: 90657770 CANCERLIT
DOCUMENT NUMBER: 90657770
TITLE: INITIAL CLINICAL TRIAL OF MURAMYL TRIPEPTIDE DERIVATIVE (**MTP-PE**) ENCAPSULATED IN LIPOSOMES: AN INTERIM REPORT.
AUTHOR: Creaven P J; Brenner D E; Cowens J W; Huben R; Karakousis C; Han T; Dadey B; Adrejcio K; **Cushman M K**
CORPORATE SOURCE: Dept. of Clinical Pharmacology and Therapeutics, Roswell Park Memorial Inst., Buffalo, NY 14263.
SOURCE: UCLA Symp Mol Cell Biol, (1989). New Ser 89, pp. 297-303.
DOCUMENT TYPE: (MEETING PAPER)
FILE SEGMENT: ICDB
LANGUAGE: English
ENTRY MONTH: 199001
AB **MTP-PE** (CGP 19835A) encapsulated in liposomes is a synthetic muramyl tripeptide coupled to dipalmitoylphosphatidyl-ethanolamine. It is N-acetylmuramyl-L-alanyl-D-isoglutaminyl-L-alanine-2 (1,2-dipalmitoyl-sn-glycero-3-[hydroxyphosphoryloxy]) ethylamide monosodium salt, encapsulated in a multilamellar liposome formed from phosphatidylcholine and phosphatidylserine in a molar ratio of 7:3. On the basis of its ability to activate macrophages to the tumoricidal state and its antitumor activity when given systemically, the compound was introduced into a Phase I clinical trial. The starting dose was 0.01 mg/m2 per dose, given by 1-hr infusion in 50 ml of isotonic saline through a safety filter, twice a week for a total of 8 doses. In the presence of stable disease or tumor response, a further course or courses was given, but no intrapatient drug escalation was carried out. The following dose

levels (mg/m2) were evaluated: 0.01, 0.05, 0.1, 0.2, 0.4, 0.8, 1.2, and 1.8. Twenty-five patients (pts; 17 men, 8 women; median age: 56 yr, range: 18-75 yr) with solid tumors resistant to conventional therapy were entered into the study. Tumors were mainly renal cell carcinoma (10) and melanoma (3). A number of acute systemic toxicities were seen; fever and rigors were the most prominent. There appeared to be relatively little dose-response relationship in these toxicities. However, toxicity was often more severe after the first than after subsequent doses. No alterations in hematologic or biochemical parameters were noted in any pt.

Macrophage activation was extremely variable from pt to pt and from dose to dose in the same pt. One pt with renal cell carcinoma with multiple small pulmonary metastases showed a diminution in the size of the lesions after one course and further diminution after two courses. After three courses, the lesions could no longer be identified on computerized tomography scan. This drug was well tolerated on a twice weekly schedule for 4 wk. The pt acceptance was high and dose-limiting toxicity was reached. The study is continuing. (6 Refs)

L4 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1989:258404 BIOSIS
DOCUMENT NUMBER: BR36:125628
TITLE: INITIAL CLINICAL TRIAL OF MURAMYL TRIPEPTIDE DERIVATIVE **MTP-PE** ENCAPSULATED IN LIPOSOMES AN INTERIM REPORT.
AUTHOR(S): CREAVEN P J; BRENNER D E; COWENS J W; HUBEN R; KARAKOUSIS C; HAN T; DADEY B; ADREJCIO K; **CUSHMAN M K**
CORPORATE SOURCE: DEP. CLIN. PHARMACOL., NEW YORK STATE DEP. HEALTH, BUFFALO, NEW YORK, 14263.
SOURCE: LOPEZ-BERESTEIN, G. AND I. J. FIDLER (ED.). UCLA (UNIVERSITY OF CALIFORNIA-LOS ANGELES) SYMPOSIA ON MOLECULAR AND CELLULAR BIOLOGY NEW SERIES, VOL. 89. LIPOSOMES IN THE THERAPY OF INFECTIOUS DISEASES AND CANCER; LAKE TAHOE, CALIFORNIA, USA, FEBRUARY 16-20, 1988. XX+480P. ALAN R. LISS, INC.: NEW YORK, NEW YORK, USA. ILLUS, (1989) 0 (0), 297-304.
CODEN: USMBD6. ISSN: 0735-9543. ISBN: 0-8451-2688-1.
FILE SEGMENT: BR; OLD
LANGUAGE: English

L4 ANSWER 3 OF 3 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1988:327294 BIOSIS
DOCUMENT NUMBER: BR35:32628
TITLE: PHASE I STUDY OF **MTP-PE** ENCAPSULATED IN LIPOSOMES.
AUTHOR(S): CREAVEN P J; BRENNER D E; COWENS J W; DADEY B; HUBEN R; KARAKOUSIS C; ARBUCK S; **CUSHMAN M K**; HAN T; ANDREJCIO K
CORPORATE SOURCE: ROSWELL PARK MEMORIAL INST., BUFFALO, N.Y.
SOURCE: SYMPOSIUM ON LIPOSOMES IN THE THERAPY OF INFECTIOUS DISEASES AND CANCER HELD AT THE 17TH ANNUAL MEETINGS OF THE UCLA (UNIVERSITY OF CALIFORNIA-LOS ANGELES) SYMPOSIA ON MOLECULAR AND CELLULAR BIOLOGY, LAKE TAHOE, CALIFORNIA,

USA, FEBRUARY 16-20, 1988. J CELL BIOCHEM SUPPL, (1988) 0 (12 PART B), 262.
CODEN: JCBSD7.
DOCUMENT TYPE: Conference
FILE SEGMENT: BR; OLD
LANGUAGE: English

=> s MTP-PE

L5 552 MTP-PE

=> d ti 1

L5 ANSWER 1 OF 552 MEDLINE
TI Maintenance of intestinal epithelium structural integrity and mucosal leukocytes during chemotherapy by oral administration of muramyl tripeptide phosphatidylethanolamine.

=> s l5 and T-cell or B-cell
<------User Break------>
u
SEARCH ENDED BY USER

=> s l5 and (antibod? or T-cell)

2 FILES SEARCHED...
L6 99 L5 AND (ANTIBOD? OR T-CELL)

=> s l6 and py<1997

2 FILES SEARCHED...
L7 93 L6 AND PY<1997

=> s l7 and B-cell

2 FILES SEARCHED...
L8 5 L7 AND B-CELL

=> dup rem l8

PROCESSING COMPLETED FOR L8
L9 2 DUP REM L8 (3 DUPLICATES REMOVED)

=> d ibib abs 1-2

L9 ANSWER 1 OF 2 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 94219166 MEDLINE
DOCUMENT NUMBER: 94219166
TITLE: Disposition of antigen-presenting liposomes in vivo: effect
on presentation of herpes simplex virus antigen rgD.
AUTHOR: Ho R J; Burke R L; Merigan T C
CORPORATE SOURCE: Department of Pharmaceutics, University of Washington School of Pharmacy, Seattle 98195.
CONTRACT NUMBER: AI 28685 (NIAID)

AI 31854 (NIAID)
SOURCE: VACCINE, **(1994)** 12 (3) 235-42.
Journal code: X6O. ISSN: 0264-410X.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199407

AB Antigen-presenting liposomes (APLs) containing a lipophilic derivative of muramyl tripeptide (**MTP-PE**) have previously been shown to enhance the immunotherapeutic effects mediated by HSV recombinant protein gD (rgD) after HSV type 2 infection is established. In this study, both the in vivo disposition of rgD and the immunological activity of in vivo-delivered rgD were determined. Following intravenous administration, most of the liposome-encapsulated rgD accumulated rapidly, mainly in the spleen, while most of the soluble rgD was quickly eliminated through the kidney. We have compared the **T-cell** stimulatory effects of macrophages, **B cells** and dendritic cells from the spleens of animals treated with rgD in vivo. Of these antigen-presenting cells, only adherent macrophages, isolated from the spleens of animals treated with rgD encapsulated in APLs for 90 minutes, were capable of stimulating HSV-sensitized autologous T and **B cells**. Additional in vitro exposure of macrophages to rgD was not required. In contrast, spleen macrophages from HSV-sensitized animals exposed to either empty liposomes or free rgD did not exhibit such immune responses, indicating that the immunobiological effect of the rgD delivered in APLs is antigen- and carrier-specific. The enhanced delivery of antigen to spleen cells, coupled with **MTP-PE** immunostimulatory activity, may be the key factors for the enhanced therapeutic effects observed in treating HSV-2 disease in guinea pigs. This approach will be useful to enhance the induction of secondary immune responses in postinfection vaccination schemes.

L9 ANSWER 2 OF 2 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 89090255 MEDLINE
DOCUMENT NUMBER: 89090255
TITLE: Control of IgE responses.
AUTHOR: Durkin H G; Auci D L; Chice S M; Smith M C; Murali M R; Bazin H; Tarcsay L; Dukor P
CORPORATE SOURCE: Department of Pathology, State University of New York Health Science Center, Brooklyn 11203..
SOURCE: CLINICAL IMMUNOLOGY AND IMMUNOPATHOLOGY, **(1989 Jan)** 50 (1 Pt 2) S52-72.
Journal code: DEA. ISSN: 0090-1229.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198904

AB Peyer's patches (PP) in germ-free rats (GF) and in the hyper-IgE syndrome patient (HIES) differ from their conventional rat (C) and healthy human (HH) counterparts in that GF rats contained fewer (two-fold) PP and none was detected in HIES. Existing PP in GF rats had reduced cellularity (three-fold) and different B and **T cell** subsets: high numbers of IgE-bearing (sIgE+) **B cells** (approximately 15% of total cells), one-half of which also expressed sIgA, were present in GF rat PP while none was detected in C rat PP (less than 1%). GF rat PP

also contained elevated numbers of sIgA+ cells and decreased sIgM+ cells, with elevated numbers of sThy 1+ RT 7.1+ Ig- **T cells** (suppressor phenotype) and reduced sThy 1- RT 7.1+ Ig- **T cells** (helper phenotype). The cellular composition of GF rat PP was converted to that resembling a C rat within 18 hr after (a) use of standard (unautoclaved) chow; (b) feeding with certain bacteria or "working" bacterial cell wall components (BCWC) and synthetic derivatives, murein, **MTP-PE**, and norMDP, but not with LPS, core lipid A, or lipoprotein; BCWC had no effect if injected intravenously; or (c) thymectomy. Each procedure resulted in (i) elimination of sIgE+ **B cells** and normalization of the other isotypes, and (ii) loss of T suppressor cells and normalization of T helper cells. After treatments, no sIgE+ cells were detected in bone marrow (BM), thymus, other lymphoid organs, or blood. PP were not detected in HIES, although they were present in HH (approximately 10/individual). P blood contained two distinct sIgE+ **B cell** subpopulations, the apparent source of which was mesenteric lymph node (MLN), the only organ in which high numbers of these cells (35%) (five nodes examined) were detected; far fewer IgE+ cells were found in spleen (less than 5%), and none was detected in BM, thymus, other LN, or appendix, which was virtually acellular. Virtually no IgE secreting plasma cells were detected in MLN, spleen, appendix, other lymphoid organs, or in gut lamina propria. IgE+ **B cells** in MLN were not detected in follicles (classical **B cell** areas); instead, they were found in high numbers in the thymus-dependent area and in medulla. Most follicles (greater than 98%) in MLN and spleen contained intercellular IgE complexed to bacterial antigen and/or CD23 (IgE-binding factor? antigen?), but contained no germinal centers.(ABSTRACT TRUNCATED AT 400 WORDS)

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(FILE 'HOME' ENTERED AT 11:12:53 ON 20 JUL 2000)

FILE 'MEDLINE, CANCERLIT, EMBASE, BIOSIS' ENTERED AT 11:13:12 ON 20 JUL 2000

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L1            0 S N-ACETYLMURAMYL-L-ALANYL-DISOGLUTAMINYL?
L2          423 S CUSHMAN-M?/AU
L3            3 S L2 AND MTP-PE
L4            3 DUP REM L3 (0 DUPLICATES REMOVED)
L5          552 S MTP-PE
L6           99 S L5 AND (ANTIBOD? OR T-CELL)
L7           93 S L6 AND PY<1997
L8            5 S L7 AND B-CELL
L9            2 DUP REM L8 (3 DUPLICATES REMOVED)
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=> dup rem l6

PROCESSING COMPLETED FOR L6

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L10          45 DUP REM L6 (54 DUPLICATES REMOVED)
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=> s l10 and cancer

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L11           8 L10 AND CANCER
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=> d ibib abs 1-8

L11 ANSWER 1 OF 8 MEDLINE
ACCESSION NUMBER: 96159395 MEDLINE
DOCUMENT NUMBER: 96159395
TITLE: In vitro and in vivo production of interleukin-6 induced by muramyl peptides and lipopolysaccharide in normal dogs.
AUTHOR: Shi F; Kurzman I D; MacEwen E G
CORPORATE SOURCE: Department of Medical Sciences, School of Veterinary Medicine, University of Wisconsin-Madison 53706, USA.
SOURCE: CANCER BIOTHERAPY, (1995 Winter) 10 (4) 317-25. Journal code: BTN. ISSN: 1062-8401.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199606

AB Interleukin-6 (IL-6) is a multifactorial cytokine produced by many cells including monocytes and macrophages in the immune-stimulated host. We measured IL-6 activity induced by muramyl dipeptide (MDP) and lipopolysaccharide (LPS) in vitro and by liposome-encapsulated muramyl tripeptide-phosphatidylethanolamine (L-**MTP-PE**) in vivo in normal dogs. Adherent mononuclear cells were cultured with MDP, LPS, or MDP plus LPS for various time periods. After incubation, culture supernatants were collected and assayed for IL-6 activity. Sera from dogs following L-**MTP-PE** administration were also evaluated for IL-6 activity. IL-6 activity both in supernatants and sera was measured using a 7TD1 bioassay. Significantly elevated IL-6 activity could be measured as early as 2 hours after mononuclear cells were exposed to MDP, LPS, or MDP plus LPS. IL-6 activity induced by LPS was greater than that induced by MDP, and the combination of MDP and LPS induced the greatest increase in IL-6 activity. Serum IL-6 activity was elevated within 3 to 4 hours post L-**MTP-PE** administration and subsequently declined to pretreatment level at 24 hours post injection. Neutralization of supernatant and serum IL-6 activity was not achieved with goat or rabbit anti-recombinant human IL-6 polyclonal **antibody**. This study demonstrates that MDP and LPS, alone and in combination, can induce enhanced IL-6 activity of canine adherent mononuclear cells in vitro, and that intravenous injection of L-**MTP-PE** is capable of eliciting increased IL-6 activity in vivo in normal dogs. These findings suggest that IL-6 may play an important role in the biologic response observed in canine **cancer** patients treated with L-**MTP-PE**.

L11 ANSWER 2 OF 8 MEDLINE
ACCESSION NUMBER: 94148576 MEDLINE
DOCUMENT NUMBER: 94148576
TITLE: Effect of immunomodulators on specific tumor immunity induced by liposome-encapsulated tumor-associated antigens.
AUTHOR: Bergers J J; Den Otter W; Dullens H F; De Groot J W; Steerenberg P A; Filius P M; Crommelin D J
CORPORATE SOURCE: Department of Pharmaceutics, Utrecht Institute for Pharmaceutical Sciences, University of Utrecht, The Netherlands..

SOURCE: INTERNATIONAL JOURNAL OF CANCER, (1994 Mar 1) 56 (5) 721-6.
Journal code: GQU. ISSN: 0020-7136.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199405

AB Reconstituted membranes consist of liposomal structures formed by removal of detergent from solubilized membrane constituents. The membrane-like configuration of reconstituted membranes makes them attractive as vehicles for presentation of tumor-associated antigens and induction of immune responses. In this study the potential of immunomodulators was assessed to enhance the specific immune response induced by immunization with reconstituted membranes prepared from SL2 lymphosarcoma cells. Reconstituted membranes containing muramyl tripeptide phosphatidylethanolamine (**MTP-PE**) provided better protection against a challenge with SL2 cells than did reconstituted membranes containing alternative immunomodulators. Local administration of IL-2 at the immunization sites further augmented the protection induced by reconstituted membranes with **MTP-PE**, but was ineffective when administered with plain reconstituted membranes. Immunity elicited by the triple modality of reconstituted SL2 membranes with **MTP-PE** and IL-2 was specific for SL2 cells. Systemic immunity was obtained against a challenge with a 100-fold higher number of SL2 cells than was reached after immunization with reconstituted membranes alone (10(5) vs. 10(3) SL2 cells). Macrophages isolated from the peritoneal cavity of immunized mice 5 to 7 days after tumor challenge expressed high in vitro cytotoxicity. However, in contrast to the observed specificity of the systemic immunity, macrophages killed both SL2 cells and non-related P815 cells. Neither major cytotoxic lymphocyte activity nor substantial cytotoxic **antibody** titers were detectable. These results clearly indicate that the approach using reconstituted membranes combined with particular immunomodulators warrants further exploration for the development of safe, well-characterized **cancer** vaccines.

L11 ANSWER 3 OF 8 MEDLINE
ACCESSION NUMBER: 93364895 MEDLINE
DOCUMENT NUMBER: 93364895
TITLE: In vitro and in vivo effect of doxorubicin combined with liposome-encapsulated muramyl tripeptide on canine monocyte activation.
AUTHOR: Shi F; MacEwen E G; Kurzman I D
CORPORATE SOURCE: Department of Medical Sciences, School of Veterinary Medicine, University of Wisconsin, Madison 53706.
SOURCE: CANCER RESEARCH, (1993 Sep 1) 53 (17) 3986-91.
Journal code: CNF. ISSN: 0008-5472.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199312

AB Chemotherapeutic agents have been shown to enhance the antitumor activity of biological response modifiers and cytokines in rodents and humans. The purpose of this study was 2-fold: (a) to determine whether doxorubicin (DOX) would enhance or interfere with the effect of muramyl dipeptide and lipopolysaccharide on canine monocyte activation as measured by an in vitro WEHI-164 cell cytotoxicity assay; and (b) to evaluate the in vivo effect of DOX alone and combined with liposome-encapsulated muramyl tripeptide-phosphatidylethanolamine (L-**MTP-PE**) on monocyte activation and serum tumor necrosis factor activity. The in vitro results showed that increasing concentrations of DOX for either 1 or 24 h incubation did not directly enhance or inhibit spontaneous or activated monocyte supernatant-mediated cytotoxicity. The in vivo study showed that monocyte supernatant-mediated cytotoxicity was increased on day 3 and significantly elevated on day 7 ($P = 0.016$) post-DOX (30 mg/m2, single injection) administration. When DOX was given in combination with L-**MTP-PE** (2 mg/m2, twice weekly for 3 weeks), monocyte-mediated cytotoxicity was enhanced on days 3 through 10 with a significant increase on day 10 ($P < 0.001$). In vivo monocyte supernatant-mediated cytotoxicity was significantly elevated in dogs receiving L-**MTP-PE** alone at 2 h after day 0, 7, and 14 treatment, and this response was further enhanced by DOX. Serum tumor necrosis factor activity at 2 h post-L-**MTP-PE** was enhanced and sustained for a longer period of time in dogs that also received DOX. We conclude that DOX administered with L-**MTP-PE** will enhance canine monocyte activation induced by DOX or L-**MTP-PE** alone, and suggest that DOX may be combined with L-**MTP-PE** early in the treatment of **cancer** patients.

L11 ANSWER 4 OF 8 MEDLINE
ACCESSION NUMBER: 90257641 MEDLINE
DOCUMENT NUMBER: 90257641
TITLE: Interleukin-6 induction by a muramyltripeptide derivative in **cancer** patients.
AUTHOR: Frost H; Murray J L; Chaudri H A; Van Damme J
CORPORATE SOURCE: Research and Development and Medical Statistics, CIBA-GEIGY Limited, Basel, Switzerland.
SOURCE: JOURNAL OF BIOLOGICAL RESPONSE MODIFIERS, (1990 Apr) 9 (2) 160-6.
Journal code: JBM. ISSN: 0732-6580.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199008

AB Interleukin-6 (IL-6) was measured in sera from 26 patients with advanced malignancies before and after an I.V. infusion of muramyltripeptide-phosphatidylethanolamine (MPT-PE) in liposomes. Significantly elevated IL-6 could be measured 2 and 4 h after medium (0.25-0.5 mg/m2) and high (1.0-6.0 mg/m2) doses of the drug accompanied by a rise in body temperature. The biological activity of IL-6 in sera could be inhibited in vitro by monoclonal **antibodies** against IL-6. Other biological effects of **MTP-PE** in vivo such as leukocytosis and

elevated acute phase reactants are discussed in view of increased IL-6 levels. It is concluded that **MTP-PE** in liposomes generates increased amounts of IL-6 measurable in serum several hours after administration. IL-6 could therefore play an important role in the biological response modification induced by the drug.

L11 ANSWER 5 OF 8 CANCERLIT
ACCESSION NUMBER: 91668615 CANCERLIT
DOCUMENT NUMBER: 91668615
TITLE: COMBINING BIOLOGICAL RESPONSE MODIFIERS WITH CYTOTOXICS IN THE TREATMENT OF **CANCER**: DEVELOPING A RATIONAL APPROACH TO A NEW THERAPY. MARCH 5-7, 1990, BALTIMORE, MD.
AUTHOR: Anonymous
CORPORATE SOURCE: No affiliation given.
SOURCE: Non-serial, (1990). Combining Biological Response Modifiers with Cytotoxics in the Treatment of Cancer:Developing a Rational Approach to a New Therapy. March 5-7, 1990, Baltimore, MD, NCI, 1990. :.
DOCUMENT TYPE: Book; (MONOGRAPH)
FILE SEGMENT: ICDB
LANGUAGE: English
ENTRY MONTH: 199103
AB The meeting on combining biologic response modifiers (BRMs) with cytotoxics in the treatment of **cancer**, held March 5-7, 1990, in Baltimore, MD, had as its theme developing a rational approach to a new therapy and presented topics in five sessions. Introductory remarks concerned anticancer drugs and BRM action--the example of Adriamycin. Session I, on enhancement of BRM antitumor activity by cytotoxic agents, included these topics: ways in which cytotoxic agents can enhance the activity of BRMs, potentiation of the human immune response by cyclophosphamide, and influence of chemotherapy on monocyte activation by the biologic agent liposomal **MTP-PE**. Session II, on enhancement of cytotoxic antitumor activity by BRMs, included influences on chemotherapy efficacy of interleukin-1 alpha-induced pathophysiologies in solid tumors and synergistic antitumor effects of topoisomerase inhibitors, natural cell-mediated cytotoxicity, and tumor necrosis factor.
Session III, on preclinical evaluation and clinical correlation of drug/BRM interactions, presented the following: preclinical and clinical development of flavone acetic acid plus IL-2 for **cancer** treatment, use of a human tumor cloning system to identify potentially synergistic combinations of biologic and cytotoxic agents, interaction of gamma interferon (IFN) and 5-fluorouracil (5FU) in the H630 human colon carcinoma line, clinical and preclinical interactions of recombinant alpha-2a IFN and 5FU, mathematical modeling of drug/BRM interactions, tumor regression through **T-cell** depletion, and strategies for combining drugs and BRMs using animal tumor models. Session IV addressed regulatory considerations in the development of drug/BRM combinations, and Session V was a round-table discussion of future directions. Posters available for viewing were discussed at the end of Sessions II and III.

L11 ANSWER 6 OF 8 CANCERLIT
ACCESSION NUMBER: 89657438 CANCERLIT
DOCUMENT NUMBER: 89657438
TITLE: BIOLOGICAL RESPONSE MODIFIERS.

AUTHOR: Clark J W
CORPORATE SOURCE: Biological Response Modifiers Program, Clinical Res. Branch, Div. of Cancer Treatment, NCI-Frederick Cancer Res.
Facility, Frederick, MD 21701.
SOURCE: Cancer Chemother Biol Response Modif, (1988). Vol. 10, pp. 434-59.
ISSN: 0921-4410.
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
FILE SEGMENT: ICDB
LANGUAGE: English
ENTRY MONTH: 198911

AB Biological response modifiers (BRMs) are divided into eight groups: microorganisms, chemically identified compounds from natural sources, polysaccharides, polypeptides, thymic factors, synthetic compounds, polyribonucleotides, and vaccines. Preclinical and clinical studies of BRMs are reviewed: BCG, Nocardia rubra cell wall skeleton, OK-432 (picibanil), Propionibacterium, Pseudomonas, Biostim, bryostatins, lipids, lipopolysaccharide, nutritional factors and trace metals, phototherapy (hematoporphyrin derivatives), Pseudomonas toxin, Staphylococcus protein A, PSK (Krestin), glucan, bestatin, cyclosporin A, FK-565, **MTP-PE**, neuropeptides and other neuropharmacologic agents, tuftsin, thymic factors, AS-101 (ammonium trichlorotellurate), chemotherapeutic agents (cyclophosphamide and flavone acetic acid), differentiating agents (retinoids, vitamin D compounds, and calcitriol), histamine H2-receptor blockers (cimetidine and coumarin), cyclooxygenase and lipooxygenase inhibitors, mopidamol, tamoxifen, polyribonucleotides (eg, ampligen), and vaccines. Much of the emphasis in BRM therapy over the past 5 yr has been in the evaluation of recombinant human proteins and monoclonal **antibodies**, but there are still many other agents with promise as antitumor agents. One of these, BCG, has become an accepted treatment for superficial bladder **cancer**. Most of the other BRMs are at various stages of preclinical or clinical development, and only further study will define what role, if any, they might have in the treatment of **cancer**. Preclinical animal models developed so far have been invaluable in demonstrating antitumor effects of BRMs and should be developed further. Although immunotherapy should work best when tumor burden is lowest (eg, the adjuvant setting in humans), there is currently no way of knowing which immunomodulatory agents should be evaluated in the adjuvant setting. Thus, although agents that consistently enhance the tumoricidal effects of monocytes, **T cells**, or NK cells in vivo in humans are worth considering for adjuvant trials, it is only when significant activity against metastatic disease is seen that clear decisions for use in the adjuvant setting can be made. (147 Refs)

L11 ANSWER 7 OF 8 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 2000:3151 BIOSIS
DOCUMENT NUMBER: PREV200000003151
TITLE: Squalene and squalane emulsions as adjuvants.
AUTHOR(S): Allison, Anthony C. (1)
CORPORATE SOURCE: (1) SurroMed Corporation, 1060 East Meadow Circle, Palo Alto, CA, 94303 USA
SOURCE: Methods (Orlando), (Sept., 1999) Vol. 19, No. 1, pp. 87-93.

ISSN: 1046-2023.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Microfluidized squalene or squalane emulsions are efficient adjuvants, eliciting both humoral and cellular immune responses. Microfluidization stabilizes the emulsions and allows sterilization by terminal filtration. The emulsions are stable for years at ambient temperature and can be frozen. Antigens are added after emulsification so that conformational epitopes are not lost by denaturation and to facilitate manufacture. A Pluronic block copolymer can be added to the squalane or squalene emulsion. Soluble antigens administered in such emulsions generate cytotoxic T lymphocytes able to lyse target cells expressing the antigen in a genetically restricted fashion. Optionally a relatively nontoxic analog of muramyl dipeptide (MDP) or another immunomodulator can be added; however, the dose of MDP must be restricted to avoid systemic side effects in humans. Squalene or squalane emulsions without copolymers or MDP have very little toxicity and elicit potent **antibody** responses to several anti gens in nonhuman primates. They could be used to improve a wide range of vaccines. Squalene or squalane emulsions have been administered in human **cancer** vaccines, with mild side effects and evidence of efficacy, in terms of both immune responses and antitumor activity.

L11 ANSWER 8 OF 8 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1993:525572 BIOSIS
DOCUMENT NUMBER: PREV199396138979
TITLE: Activation of cytolytic activity in peripheral blood monocytes of renal **cancer** patients against non-cultured autologous tumor cells.
AUTHOR(S): Galligioni, Enzo (1); Quaia, Michele; Spada, Antonella; Favaro, Daniela; Santarosa, Manuela; Talamini, Renato; Monfardini, Silvio
CORPORATE SOURCE: (1) Div. Oncologia Medica, Centro Riferimento Oncologico, Via Pedemontana Occidentale, 33081 Aviano Italy
SOURCE: International Journal of Cancer, (1993) Vol. 55, No. 3, pp. 380-385.
ISSN: 0020-7136.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Our purpose was to evaluate the ability of blood monocytes of renal **cancer** patients to become cytotoxic against fresh, autologous tumor cells. Fresh target cells were obtained by mechanical and enzymatic dissociation of tumor and normal renal tissue. The A375 cell line, derived from a human melanoma, and the SW626 cell line, derived from a human ovarian carcinoma, were used as positive target cell controls. Monocytes from renal **cancer** patients and normal volunteers were activated in vitro with lipopolysaccharide (LPS), or muramyl tripeptide (**MTP -PE**), or multilamellar vesicle liposomes containing **MTP -PE** (MLV-**MTP-PE**), with or without a pre-incubation with r-IFN-gamma, and tested for cytotoxicity in a 72-hr 111Indium-release assay. All patients were tumor-free at the time of the monocyte study. No difference in cytotoxic activity was observed between monocytes from healthy volunteers and those from **cancer** patients. Freshly dissociated tumor cells were as susceptible to

tumoricidal monocytes as the 2 cell lines. Moreover, no cell population appeared to be resistant to activated monocytes, which were cytotoxic to both allogeneic and autologous fresh tumor cells. Activated monocytes maintained their ability to discriminate between normal and neoplastic cells and were not cytotoxic against autologous or allogeneic normal non-neoplastic cells. Our data indicate that MLV **MTP-PE** liposomes activate peripheral blood monocytes from **cancer** patients to a tumoricidal status against fresh, dissociated non-cultured autologous tumor cells.

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FULL ESTIMATED COST	18.93	19.08

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